REMARKS

I. Rejection of Claims 4, 6, 9, 11, 24, 26, 27, 29, 66-70, and 72-74 Under 35 U.S.C. §103

A) The Claimed Compositions Prevent T Cell Activation

The Examiner rejected Claims 4, 6, 9, 11, 24, 26, 27, 29, 66-70, and 72-74 Under 35 U.S.C. §103 as being unpatentable over Bona et al. and Kuchroo et al. on the assertion that the prior art suggested that the claimed compositions would "inactivate T cells for an extended period of time" However, in the office action mailed March 21, 2001, the Examiner acknowledged that the prior art would not have reasonably predicted that the claimed compositions prevent T cell activation. As amended herein, Claim 66 recites that the claimed compositions prevent T cell activation.

Support for the amended language can be found, for example, in page 16, line 31 of the specification and on page 12, lines 8-11, where the prevention of T cell activation is described

The Applicant has demonstrated the prevention of T cell activation by the claimed composition. For instance, Example 8 demonstrates *in vitro* prevention of T cell activation (see Figure 5). Antigen presenting cells were incubated with an agonist (either PLP1, IgPLP1, or PLP) in combination with various concentrations of antagonist (such as IgPLP-LR or PLP-LR). The antigen presenting cells were then mixed with T cells responsive to the agonist PLP1. T cell activation was evaluated by determining the amount of IL-2 produced by the T cells (Il-2 is produced by activated T cells but not by T cells which have not been activated). IL-2 levels were assessed by evaluating proliferation of the IL-2 responsive cell line HT-2 using ^{3}H thymidine. Accordingly, high levels of thymidine incorporation in the HT-2 cells would have indicated T cell activation. However, IgPLP-LR addition greatly reduced the levels of thymidine incorporation. These results demonstrate that the claimed compositions prevent T cell activation.

Further demonstrations that the claimed compositions prevent T cell activation can be found in the Declaration submitted by Habib Zaghouani on March 29, 2000. An experiment is described in which the administration of IgPLP-LR permanently eliminated disease symptoms in mice suffering from EAE (Exhibit B). If T cell activation occurred after treatment with the claimed compositions, the symptomatic mice would have relapsed or remained symptomatic during the 17 week test period. However, mice treated with the claimed compositions no longer

exhibited disease symptoms, and did not relapse as did the control mice. Therefore, the claimed compositions prevented T cell activation.

Furthermore, Example 9 demonstrates that the claimed compositions work by preventing T cell activation rather than simply competing for binding to the Fc receptor. This is demonstrated by showing that IgPLP-LR (which contains a T cell receptor antagonist) prevents proliferation of HT-2 cells in the assay described in Example 8, but IgPLP2 (which contains a segment of the PLP protein which is not a T cell receptor antagonist) does not prevent proliferation of HT-2 cells. Since IgPLP2 can bind to the Fc receptor, this result demonstrates that the claimed compositions do not act by competing for the Fc receptor but rather by preventing T cell activation.

B) Prevention of T Cell Activation is an Unexpected Result

As acknowledged by the Examiner in the office action mailed March 21, 2001, the prevention of T cell activation by the claimed compositions is clearly a new and unexpected result. As indicated by Exhibit B of the declaration submitted on March 29, 2000, and the Examples discussed above, the claimed compositions prevent T cell activation. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §103 be withdrawn.

II. Rejection of Claims 4, 6, 9, 11, 24, 26, 27, 29, 66-70, and 72-74 Under 35 U.S.C. §112

The Examiner rejected claims 4, 6, 9, 11, 24, 26, 27, 29, 66-70, and 72-74 Under 35 U.S.C. §112, on the assertion that the Applicant has no written support in the originally filed claims or specification for the phrase "thereby inactivating T cells for an extended period of time." Although Applicants maintain that this phrase is supported in the specification, to address the Examiner's concerns, the language " inactivating T cells for an extended period of time" has been deleted from Claim 66 and replaced with "preventing T cell activation". Support for the amended language can be found, for example, in page 16, line 31 of the specification, as discussed above. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §112 be withdrawn.

III. Rejection of Claims 9, 11, 24, 26, 27, 29, 66-68, 70, and 72 Under 35 U.S.C. §102

The Examiner rejected claims 9, 11, 24, 26, 27, 29, 66-68, 70, and 72 Under 35 U.S.C. §102 as being anticipated by Liu et al. (*J. Clin. Invest.* 98:2000-2007, 1996). The accompanying Declaration under 37 CFR 1.131 demonstrates that the inventor, Habib Zaghouani, completed the

invention prior to November 1996, the publication date of the Liu reference. Therefore, the Applicant respectfully requests that the rejection under 35 U.S.C. §102 be withdrawn.

IV. Conclusion

In view of the above, Applicant respectfully submits that the claims are in condition for allowance. Should the Examiner have any questions regarding this matter he is invited to telephone the undersigned so that the questions may be resolved.

The specific changes to the specification and the amended claims are shown on a separate set of pages attached hereto and entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this Amendment. On this set of pages, the insertions are double underlined while the ~~deletions are stricken through~~.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: Sept. 20, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIM:

66. (previously amended three times) A composition comprising an immunoglobulin or a portion thereof linked to a protein fragment or peptide, wherein said immunoglobulin or portion thereof is capable of binding to an Fc receptor and said protein fragment or peptide comprises a T cell receptor antagonist, said composition having the property of being endocytosed by cells bearing said Fc receptor and processed by the cells to present said T cell receptor antagonist in association with endogenous MHC Class II molecules, thereby ~~inactivating T cells for an extended period of time~~ preventing T cell activation.

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